PATENT SPECIFICATION (11) 1360536 GB

1360536

(21) Application No. 19500/72 (22) Filed 25 April 1972

(23) Complete Specification filed 30 March 1973

(44) Complete Specification published 17 July 1974

(51) International Classification C07D 31/42 A61K 27/00

(52) Index at acceptance

C2C 1530 215 247 250 251 25Y 292 29Y 30Y 322 32Y 360 361 365 366 367 36Y 43X 452 45X 45Y 620 633 638 650 652 658 672 682 790 79Y LU

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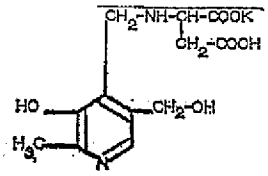
(19)

(54) PYRIDOXYL-*l*-ASPARTIC ACID SALT

(71) We, SOCIETE D'ETUDES DE PRODUITS CHIMIQUES, a company organised and existing under the laws of France, of 16 rue Kleber 92130 Issy-Less-Moulineaux, France, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to mono-potassium-pyridoxyl aspartate, to a method for its manufacture and to therapeutic compositions containing it.

The mono-potassium-pyridoxyl-*l*-aspartate of the invention has the formula I;



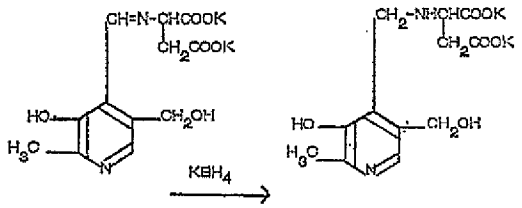
I

This compound is a white powder melting at 240°C to 245°C, soluble in water, insoluble in chloroform and in ethanol. The pH of an aqueous solution containing 5% of this product is 5.7.

The invention also provides a method for preparing the above compound, comprising reacting pyridoxal, preferably in solution in methanol, with dipotassium-l-aspartate; hydrogenating the resulting Schiff's base with potassium borohydride KBH_4 and converting the resulting di-potassium salt into the mono-potassium salt by an appropriate addition of a mineral acid.

By using potassium borohydride as the hydrogenating agent it is possible to obtain a yield of about 66%.

The hydrogenation step proceeds according to the following reaction scheme:



Pharmacological experiments have shown satisfactory cardiac analeptic action at doses from 20 mg/kg. I.V. on anaesthetized dogs and an anti-fibrillary action at doses from 100 mg/kg I.P., on mice by the technique of Lawson. The invention accordingly provides a therapeutic composition comprising the salt according to the invention in admixture with an inert diluent or carrier, suitably in unit dosage form.

The following Example illustrates the invention.

Example

In a 10 litre reactor there were poured 5 litres of dried methanol and 112 g of potassium hydroxide. The reactor was heated to 30°C and there were added 133.1 g of aspartic acid whilst stirring. 15 minutes later there were added, whilst stirring,

167.2 g of pyridoxal and stirring was maintained for one hour at room temperature to obtain a yellow solution. The reaction mixture was then heated to 30°C, there were slowly added 13.5 g of potassium borohydride, whilst stirring, and the reaction mixture was maintained for 2 hours at room temperature. The colourless solution thus obtained was cooled in an ice bath and there were added 30 g of acetic acid dissolved in a sufficient amount of water to give 240 ml of solution. The water added served to effect the degradation of the non-reacted potassium borohydride. Stirring was maintained for one hour and there were added 440 g of acetic acid diluted in methanol to give 1 litre of solution. The mixture was stirred for 2 days.

There was obtained a white precipitate which was separated, washed with methanol, rinsed with diethyl ether and then dried.

Yield: 215 g (66%).

WHAT WE CLAIM IS:—

1. Mono-potassium-pyridoxyl-*l*-aspartate of the formula I herein.

2. A process for the preparation of mono-potassium-pyridoxyl-*l*-aspartate consisting in reacting pyridoxal with di-potassium-*l*-aspartate, hydrogenating the resulting base with potassium borohydride and converting the resulting di-potassium salt into the corresponding mono-potassium salt by an appropriate addition of mineral acid.

3. A process according to claim 2, wherein the pyridoxal is reacted with the di-potassium-*l*-aspartate in solution in methanol.

4. A process for the preparation of mono-potassium-pyridoxy-*l*-aspartate substantially as described in the Example herein.

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Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1974.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.